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CASE STUDY

Leucine-rich α-2 glycoprotein is a predictive marker of therapeutic efficacy of the biologics in psoriatic arthritis

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The biologics are one of major therapeutic agents for psoriatic arthritis (PsA), which enables us to achieve remission. On the other hand, biologics cause side effects including infections and organ damages, and create an economic burden for patients. The less administration is demanded, still there is no definite criteria for the period of administration or the discontinuation. We have previously reported that serum leucine-rich α-2 glycoprotein (LRG) is a better biomarker for assessment of psoriasis severity compared to C-reactive protein (CRP).[1] LRG is a member of the leucine-rich repeat family and contains eight repeating consensus sequences.[2] To assess the validity of LRG predicting clinical efficacy of biologics in PsA, serum LRG were measured in PsA patients who undertook treatment with adalimumab (n = 15, 12 males and 3 females, median age 58.4 [range 17–83] years), infliximab (n = 11, 5 males and 6 females, median age 59.3 [range 42–75] years) or secukinumab (n = 10, 7 males and 3 females, median age 60.1 [range 45–86] years). Serum CRP levels and disease activity score (DAS) 28-erythrocyte sedimentation rate (ESR) as disease activity score were also examined.

After the administration of adalimumab, LRG levels rapidly decreased along with the improvement of DAS28-ESR (Figure 1A). On the other hand, CRP levels increased temporarily around 50 days after the treatment that did not correlate with the therapeutic efficacy (Figure 1A). About 150–200 days after medication, the rise of DAS28-ESR score that reflect the recurrence of disease activity was observed in accordance with the increase of serum LRG, but not CRP (Figure 1A). In addition, LRG levels already started to increase at around 100 days after treatment, which predicted the aggravation of DAS 28-ESR even before the symptom of recurrence appeared (Figure 1A). In the group treated with infliximab, both LRG and CRP levels rapidly decreased along with the improvement of DAS28-ESR (Figure 1B). However, CRP levels fluctuated between 50 and 150 days after treatment regardless of the continuous increase of DAS28-ESR (Figure 1B). In PsA patients treated with secukinumab, deterioration of DAS28-ESR at the early days corresponded better to LRG than CRP (Figure 1C). In addition, the increase of LRG reflected the recurrence of PsA after interval-prolongation of the regular secukinumab dose in one patient (Figure 1D).

The therapeutic effects of anti-tumor necrosis factor (TNF)-α antibodies were well correlated with serum LRG levels, which is consistent with the finding that LRG is induced by TNF-α in hepatocytes, neutrophils and macrophages.[3] Moreover, we previously demonstrated that LRG promotes Th17 differentiation in collagen-induced arthritis model.[4] Thus, it is likely that LRG enhances interleukin (IL)-17/IL-23 signaling in PsA through recruitment of infiltrating cells to the lesion. Good correspondence of serum LRG with DAS-28 ESR in PsA patients receiving secukinumab suggests

All authors contributed equally to this work.

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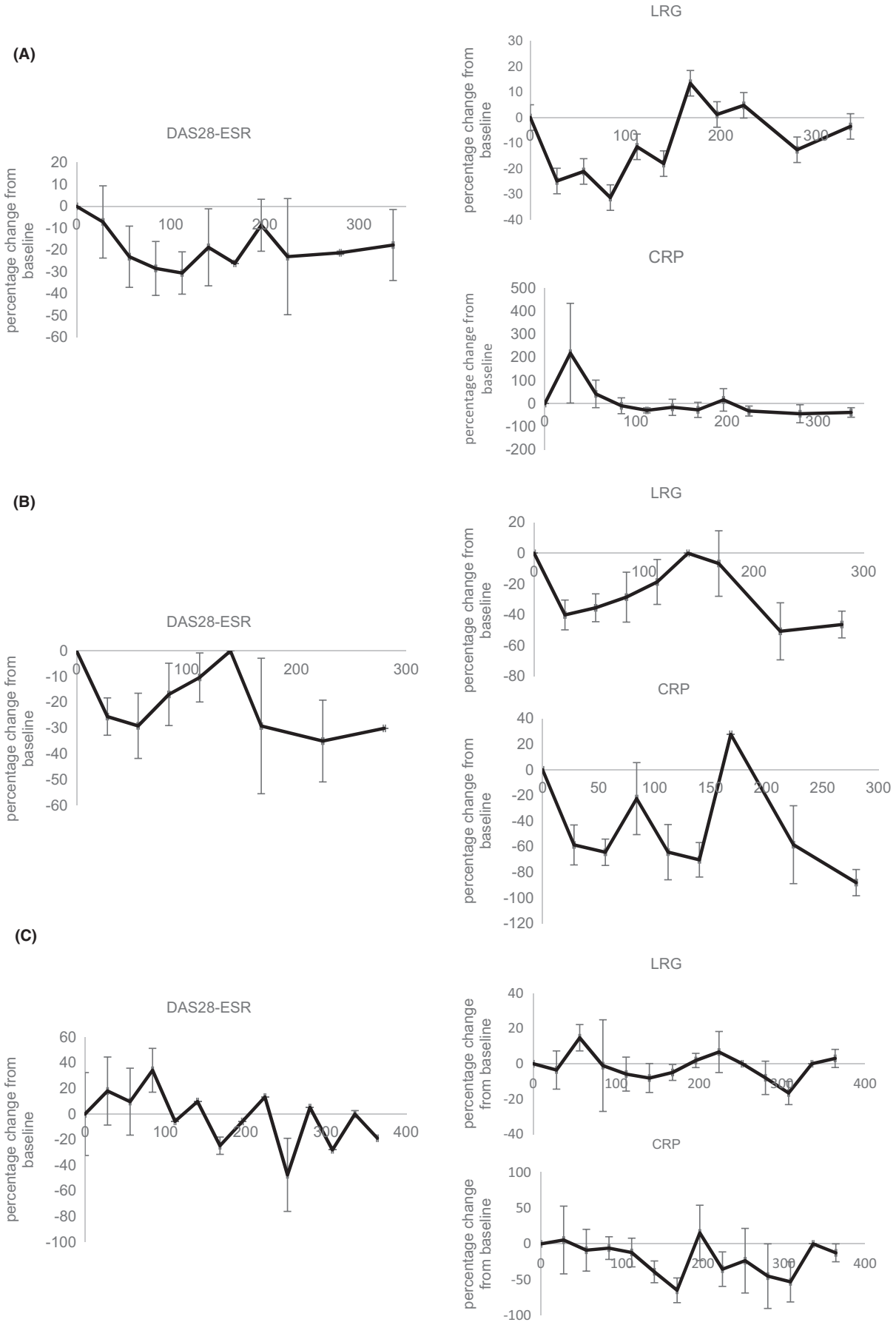

FIGURE 1 (Continued)

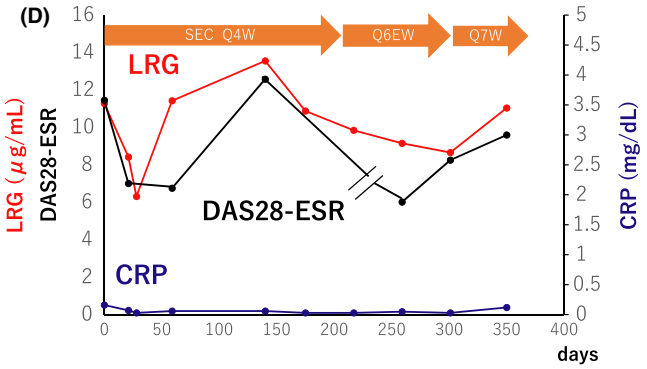

FIGURE 1 A–C, The percentage change ratio from baseline of LRG, CRP, and DAS28-ESR after the administration of biologics. A, adalimumab (*n* = 15, 12 males and 3 females, median age 58.4 [range 17–83] years), B, infliximab (*n* = 11, 5 males and 6 females, median age 59.3 [range 42-75] years), C, secukinumab (*n* = 10, 7 males and 3 females, median age 60.1 [range 45–86] years). Vertical axis represents the percentage change ratio from baseline value. Horizontal axis indicates days after the initiation of treatment. Data are represented as mean ± SD. D, A 56-year-old woman with PsA who had received regular secukinumab dose interval for 7 months reduced the dose of the biologic by prolongation of the interval from every 6 weeks (Q6W) to every seven weeks (Q7W). The changes in serum levels of LRG and CRP and in DAS-28 ESR following secukinumab treatment was evaluated in this patient. SEC, secukinumab

that LRG would be a predictive marker of the efficacy of other IL-17/IL-23 biologics.

Since the biologics had been introduced into the treatment of psoriasis, remission of PsA has become possible under the biologics. We believe that LRG can be an early predictive biomarker for the efficacy of biologics in PsA.

DECLARATION SECTION

Approval of the research protocol: The protocol for this research project has been approved by a suitably constituted Ethics Committee of the institution and it conforms to the provisions of the Declaration of Helsinki. Ethics committee of the Kochi Medical School, Kochi University.

Informed consent: All informed consent was obtained from the subjects.

Registration No. of the study: 26–30.

Registry and registration No.of the study/trial: N/A.

Animal studies: N/A.

CONFLICT OF INTEREST

The authors declares no conflict of interest.

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